REMARKS/ARGUMENTS

Status of the Claims

Upon entry of the present amendment, claims 26, 35-37 and 52-69 are pending. Claims 63-67 are withdrawn and drawn to a non-elected invention. No claims are amended.

The Examiner is thanked for indicating that claim 57 is allowable and claims 35-37, 52-56, 68 and 69 are objected to.

Request for Rejoinder

Claims 63-67 are withdrawn from examination as being directed to a non-elected invention, to be examined upon determination of an allowable linking claim. In view of the arguments presented herein, Applicants believe that linking claim 26 is allowable. Accordingly, pursuant to M.P.E.P. § 821.04, Applicants respectfully request withdrawal of the restriction requirement, and examination of the withdrawn claims.

Applicants demonstrate in Example 5 on page 60 that mice deficient for the glycosyltransferase ST3GalI are deficient for CD8+ T cell function. *See*, page 60, lines 17-24 of WO 00/33076. Further disclosure regarding kits and methods for detecting T cell function deficiency is found on page 30, lines 15-31.

Telephonic Interview with the Examiner

The Examiner is thanked for graciously granting Applicants' representatives the courtesy of a telephonic interview on February 7, 2007. The issues discussed are set forth in the pending Official Action and in the present response.

Rejection under 35 U.S.C. § 102(a)

The Examiner has rejected claim 57 under 35 U.S.C. § 102(a) as allegedly anticipated by Ellies, *et al.*, *Immunity* (1998) 9:881-90 ("Ellies"). This rejection is traversed for the reasons below.

First, as discussed in the previous responses, Ellies is not prior art. U.S. Provisional Appl. No. 60/113,680 ("the 680 application") was filed before Ellies was published. The Examiner alleges that the '680 application does not teach detecting a CD45 isoform. This is incorrect.

The '680 application teaches detecting CD45 isoforms and CD43 glycoforms, as set forth in claim 58. For example, on page 6, lines 22-24, the '680 application teaches:

> **In the experiment shown in Figure 10C, splenocytes were double-stained with mAbs recognizing CD22 and the B cell specific form of CD45 (B220) or CD22 and all CD45 isoforms (30-F11). Cells were also double-stained with mAbs recognizing the 115 (S7) and 130 (1B11) kD glycoforms of CD43 and subjected to flow cytometric analysis.**

The Examiner is also respectfully directed to page 5, lines 14-16, Figure 5, Figure 10C and page 38, lines 6-8. The specification teaches that the B cell specific form of CD45 is also known as B220 (*see*, page 6, line 23 and page 38, lines 4-6). Figure 5 demonstrates the use of antibodies B220 (against B cell specific isoforms of CD45) and 1B11 (against the 130 kD glycoform of CD43) to diagnose a deficiency in the inflammatory response that results from a deficiency in Core 2 GlcNAc transferase activity.

The specification also contemplates kits that include either or both of the antibodies B220 (against B cell specific isoforms of CD45) and 1B11 (against the 130 kD glycoform of CD43 (*see*, page 24, lines 17-20). The antibodies were known by those of skill in the art and purchased from PharMingen (*see*, page 35, lines3-4).

Therefore, in view of the foregoing, the '680 application, with a filing preceding the publication of Ellies, teaches detection of detecting CD45 isoforms and CD43 glycoforms. Accordingly, Ellies is not prior art to claim 57 and the Examiner is respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 101

The Examiner has rejected claims 26 and 59-62 under 35 U.S.C. § 101 as allegedly lacking a specifically asserted to well-established utility. The Examiner alleges that use for a diagnostic reagent which specifically binds Sia6LacNac could only be ascertained for

diagnosing CDGS Ia, which is associate with a mutation which encodes a phosphomannomutase. This rejection is respectfully traversed.

Specifically-asserted utility

Applicants teach that mice deficient for the glycosyltransferase ST6GalI are deficient in proper B cell activation and function, and therefore immunodeficient. First, Applicants teach the production of mice that are deficient for ST6GalI. *See*, Figure 14 and page 9, line 3 through page 15, line 3 of WO 00/33076. As shown in Figure 14A, the genomic DNA encoding the ST6GalI glycosyltransferase is left largely intact, but does not express a functional ST6GalI enzyme because exon 2 has been excised.

ST6GalI is a glycosyltransferase that contributes to the synthesis of Sia6LacNAc. Structurally, the specification provides data showing that lymphocytes from mice deficient for ST6GalI were deficient in Sia6LacNAc. *See*, page 9, lines 28-29 and Figure 14C. *See also*, Example 4, particularly at page 54, lines 9-12. Functionally, ST6GalI deficient mice exhibited reductions in cell surface CD22 and IgM and in circulating IgM, IgG1, and IgG3. *See*, page 10, lines 14-16 and lines 25-26; Figure 15 and page 57, lines 1-8. Moreover, B cells in ST6GalI deficient mice do not activate properly: the B cells fail to mobilize intracellular Ca2+ efficiently, or generate high titers of antibodies to T cell independent antigens. See, page 56, lines 2-4, 10-11 and 29-31. Clinically, mice deficient for ST6GalI have B lymphocyte-mediated immunodeficiency. The ST6GalI-deficient mice exhibit an immunodeficient state with reduced efficacy of B lymphocyte immune activation and reduced antibody formation. *See*, page 29, lines 27-31. *See also*, Example 4, particularly at page 55, line 5 through page 57, line 8.

Therefore, Applicants have demonstrated, asserted and claimed in claims 26 and 59-62 the specific utility of detecting a deficiency in immune cell function (*e.g.*, B cells) resulting from a mutation in a glycosyltransferase gene (*e.g.*, ST6GalI). A deficiency in the glycosyltransferase ST6GalI results in the deficient production of Sia6LacNAc. Deficient production of Sia6LacNAc results in B cells that do not properly activate or produce IgM.

Well-established utility

In accordance with the telephonic discussion with the Examiner on February 7, 2007, Applicants provide evidence where the USPTO has recognized that studying mice deficient for a particular glycosyltransferase (*e.g.*, ST6GalI, ST3GalI, ST3GalIV) demonstrate patentable utility for methods of treating a pathological condition. For example, in U.S. Patent No. 6,376,475,[1] the USPTO granted claims directed to ***methods of treatment***, particularly inhibiting an immune response, including allergy, autoimmune disease, and graft rejection, based on information learned from mice with disrupted ST6GalI and ST3GalI glycosyltransferase genes. The Examiner will notice that Figures 1, 2 and 5 of the '475 patent ***are the very same*** as Figures 14-16 of the present application. In another example, the USPTO has recently allowed claims in U.S. Application No. 10/089,525 (earlier published as WO 01/22921),[2] also directed to ***methods of treatment***. The allowed claims are directed to methods of decreasing levels of von Willebrand Factor or Factor VIII based on information learned from mice with a disruption in the glycosyltransferase ST3GalIV gene.

In the present application, the claims are directed to ***methods of detection*** of a mammal with a genetically transmitted disruption in a glycosyltransferase gene that results in deficiency in immune cell function. Applicants have presented the very same data that legitimately supported claims to methods of treatment.

Moreover, detection of a genetically transmitted B-cell mediated immunodeficiency is a well-established utility. Those of skill in the art understood at the time of filing of the present application that genetically transmitted conditions that cause insufficient immunoglobulin production (*i.e.*, deficient B cell function) result in the inability to fight extracellular bacterial infections. This is supported by pages 10:11-10:16 of Janeway and Travers, *Immunobiology* (1997) Garland Publishing, New York.[3] Here, Applicants have discovered that that an etiology for B-cell mediated immunodeficiency can be genetically transmitted through a mutation in a glycosyltransferase gene, *e.g.*, a ST6GalI.

[1] U.S. Patent No. 6,376,475 is attached as Exhibit A.
[2] WO 01/22921 and the allowed claims for 10/089,525 are attached as Exhibit B.

Summary

In view of the foregoing, Applicants respectfully submit that they have asserted a specific and well-established utility. The Examiner is respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 112, first paragraph, enablement requirement

The Examiner has rejected claims 26 and 59-62 under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the enablement requirement. The Examiner alleges that without supporting either a specifically asserted or well-established utility, the skilled person would not know how to use the claimed invention. Applicants respectfully traverse.

Applicants have taught a specifically asserted and well-established utility for the reasons discussed above. Furthermore, Applicants have taught those of skill in the art how to practice the claimed methods of detection. For example, Applicants teach the use of CD22 lectin and the use of *Sambucus nigra* bark agglutinin (SNA) diagnostic reagents to detect the presence or reduced presence of Sia6LacNAc. The specification teaches that the diagnostic reagent can be tested on cells from whole blood and other tissues. *See*, page 30, lines 1-13 of WO 00/33076. Figure 3 demonstrates diagnosing a deficiency in B cell immune responses associated with a reduction of ST6GalI activity using CD22 and SNA diagnostic reagents. *See*, page 6, lines 12-14 and Figure 3. Kits for detecting Core 2 GlcNAc transferase deficiency, for example, using anti-CD45 (B220) and anti-CD43 (1B11) antibodies, are taught at page 28, lines 14-17. Kits for detecting ST3GalI deficiency, for example, using lectins peanut agglutinin (PNA), jacalin (JAC) or *Maackia amurensis* lectin (MAL II), are taught at page 30, lines 20-31.

Therefore, Applicants have shown how to practice the methods of detecting a deficiency in immune cell function (*e.g.*, myeloid cells, B cells and T cells) due to a genetically

[3] Attached as Exhibit C; made necessary by the Examiner's new rejection under 35 U.S.C. § 101.

transmitted mutation in a glycosyltransferase gene (*e.g.*, Core 2 GlcNAc, ST6GalI or ST3GalI). The Examiner is respectfully requested to withdraw this rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Jennifer L. Wahlsten
Reg. No. 46,226

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments
JLW:jlw
60986292 v1